

REMARKS

Claims 1-14 are pending. No new matter has been added by way of the present amendment. For instance, claim 11 has been clarified to remove a rejection under 35 U.S.C. § 112, second paragraph. Also, new claim 14 is supported by the present specification at page 2, line 15 to page 3, line 9 and page 6, lines 3-5. These are a non-narrowing amendments, which do not add new matter.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issues under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claim 11 under 35 U.S.C. § 112, second paragraph for the reasons recited at page 7 of the outstanding Office Action. Applicants respectfully traverse this rejection

The Examiner asserts that claim 11 is indefinite since it appears to be claiming a compound, but allegedly requires a process step. Applicants submit that claim 11 is a compound claim, and does not require a process step. Claim 11 has been amended in order to clarify this issue. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Issues under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-13 under 35 U.S.C. §103(a) as being obvious over Hong, U.S. Patent No. 5,869,670 (hereinafter referred to as "Hong '670") in view of Khomutov et al., *Tetrahedron Lett.*, 42:2887-2889 (2001) (hereinafter referred to as "Khomutov"). Applicants respectfully traverse this rejection.

The Examiner asserts that those of skill in the art would be motivated to combine the synthesis process of Gemifloxacin disclosed in Hong '670 with the use of benzaldehyde as a primary amine protecting group as disclosed in Khomutov. Applicants respectfully disagree.

As a preliminary matter, Applicants herein incorporate all arguments of record. Although the Examiner has addressed these arguments, for instance at page 4, last full paragraph of the outstanding Office Action, these arguments remain applicable. Applicants note that the Examiner asserts that claim 1 does not have a purity range in the claim; however, reference is made to claim 13, which specifically requires that an acid salt of Gemifloxacin is formed in a yield of 90% or more. Also, claim 14 specifically requires that the acid salts of Gemifloxacin represented by formula 1 prepared according to the present method contain 0.1% or less of a compound of formula 8 as an impurity.

Moreover, as previously pointed out, the present invention and Hong '670 cannot be directly compared with one another in terms of the requirement for a recrystallization step. Second, the good yields as achieved in Examples 7 and 8 of the present application (by using the intermediate of Example 1, which is not a Schiff-base type) cannot be expected from Khomutov. Third, the selective aromatic nucleophilic substitution of the secondary amine in the present invention cannot be reasonably expected from any of the cited art. Thus, the prior art fails to suggest or disclose the present method for preparing Gemafloxacin acid salts, which is characterized in that there is no step for recrystallizing Gemafloxacin, deprotection and preparation of the Gemifloxacin salt are carried out in a single step, and the aromatic nucleophilic substitution of the secondary amine occurs selectively.

Further, Applicants also stress that the Reaction Scheme 2 of Hong '670 cited by the Examiner fails to suggest or disclose the technical features of the present invention in the following points:

The Reaction Scheme 2 of Hong '670 uses a compound of formula (III') wherein amine group has been already treated with a protecting group. That is, to conduct the process of the Reaction Scheme 2 of Hong '670, an additional step to treat the primary amine formula (III) compound in the Reaction Scheme 1 with protecting group is required.

However, the present invention uses specifically a ketone or aldehyde of formula (5) to introduce amine protecting group. In the present invention, gemifloxacin salt can be prepared in a single step, without additional pre-treatment of the primary amine of formula (3) compound with protecting group.

The Examiner appears to believe that the primary amine protecting group in the present invention is derived from trifluoroacetic acid or paratoluenesulfonic acid. However in the present invention, the compound for protecting the primary amine is a ketone or aldehyde of formula (5). Also, the resulting group of combination of the primary amine and the protecting group is ketimine ($-\text{C}=\text{N}-$).

Also, in Hong '670, the primary amine protecting group, "P", is trifluoroacetyl, paratoluenesulfonyl or the like which is derived from an acid such as trifluoroacetic acid, paratoluenesulfonic acid or the like, respectively. The resulting group of combination of the primary amine such protecting acid (PHN-) has a carbonyl oxygen (e.g. in case of trifluoroacetyl, the resulting group is $\text{CF}_3-\text{C}(=\text{O})-\text{NH}-$).

Accordingly, the two inventions are clearly distinguishable from each other in the kind of the compound providing protecting group to the primary amine and the resultant structure of the primary amine after introduction of the protecting group.

In sum, the method for preparing Gemifloxacin acid salts of the present invention, wherein the step for recrystallizing Gemifloxacin is omitted, and the deprotection and preparation of Gemifloxacin salt are carried out in a single step, is clearly different from the synthesis process of Gemifloxacin comprising three steps disclosed in Hong '670 and has distinctively advantageous effects over Hong '670 in terms of yield of the target product and simplicity of the process. Khomutov cannot cure these deficiencies.

Also, the present method is clearly distinguished from Hong '670 in the kind of the compound providing protecting group to the primary amine and the resultant structure of the primary amine after introduction of the protecting group. This deficiency is not cured by Khomutov.

In view of the above, Applicants submit that it is apparent that the Examiner has failed to present a valid *prima facie* case of obviousness. Moreover, the present invention achieves unexpectedly superior results in terms of the yield of the target product and the simplicity of the process. The Examiner is therefore requested to withdraw this rejection.

Obviousness-Type Double Patenting

The Examiner has rejected claims 1-13 under the judicially created doctrine of obviousness-double patenting as being obvious over claims 1 and 2 of Hong '670 in view of Khomutov. Applicants respectfully traverse this rejection. As explained above, Applicants have distinguished claims 1-11 from the cited art. Accordingly, there exists no obviousness-type

double patenting over the combined references of Hong '670 and Khomutov. Thus, this rejection is improper and should be withdrawn.


In view of the above, Applicants respectfully submit that the present claims define subject matter which is allowable. Accordingly, the Examiner is respectfully requested to withdrawal all rejections and allow the currently pending claims.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

By 

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